Hoechst Celanese

8EHQ1094-13242

Department of
Environmental, Health &
Safety Affairs (DEHSA)

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ORIGINAL

October 21, 1994
MRS-168-94

Attn: TSCA Section 8(e) Coordinator
Document Processing Center (TS-790)
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Contains No CBI

Dear Sir or Madam:

In accordance with the requirements of TSCA Section 8(e), Hoechst Celanese hereby submits a guinea pig maximization test for propanenitrile,3-[[4-[(2,6-dichloro-4-nitrophenyl)azo]phenyl]ethylamino]-, (CAS No. 13301-61-6).

A guinea pig maximization test was conducted to assess the dermal sensitization potential of the test material. The method followed the procedure described in the OECD Guidelines for the Testing of Chemicals No. 406 "Skin Sensitization" (adopted July 1992). This method is based on that of Magnusson and Kligman, Journal of Investigative Dermatology 52, p. 268, (1969).

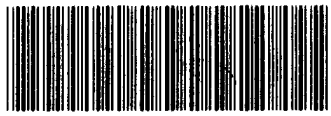
At a challenge concentration of 25% (w/w) the test material produced a 100% (10/10) positive response and was considered an extreme sensitizer to guinea pig skin under the conditions of this test.

This submission contains no confidential business information.

If any further information is required, do not hesitate to contact Dr. Michele R. Sullivan, Director, Product Stewardship at 908-231-4480.

Sincerely,

Susan P. Engelman
Vice President, Environmental, Health &
Safety Affairs



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NW4RO:

MAGNUSSON & KLIGMAN MAXIMISATION

STUDY IN THE GUINEA PIG

PROJECT NUMBER: 388/114

AUTHOR: D.J. Allen

STUDY SPONSOR:

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~~PAGE 1 OF 32 PAGES~~

Michele R. Sullivan
Recd 27 pages of this report
Per submitter. EAS

PROJECT NUMBER: 388/114

QUALITY ASSURANCE REPORT

The routine inspection of short term studies at Safepharm Laboratories is carried out as a continuous process designed to encompass all major phases of each study type once per month. Dates of the most recently completed series of monthly inspections relevant to the study type(s) in this report are given below.

Date(s) of Inspection and Reporting:

03, 04, 16, 24 May 1994

This report has been audited by Safepharm Laboratories Quality Assurance Unit. It is considered to be an accurate account of the data generated and of the procedures followed.

Date of Report Audit:

20 June 1994

J.R. Pateman C. Biol., M.I. Biol.
FOR SAFEPHARM QUALITY ASSURANCE UNIT ..... J.R. Pateman

DATE: -3. Aug. 1994 .....

GLP COMPLIANCE STATEMENT

I, the undersigned, hereby declare that the objectives laid down in the protocol were achieved and as nothing occurred to adversely affect the quality or integrity of the study, I consider the data generated to be valid. This report fully and accurately reflects the procedures used and data generated.

The work described was performed in compliance with the UK Principles of Good Laboratory Practice (The United Kingdom Compliance Programme, Department of Health 1989). These Principles are in accordance with GLP standards published as OECD Environment Monograph No. 45 (OCDE/GD(92)32); and are in conformity with, and implement, the requirements of Directives 87/18/EEC and 88/320/EEC.

These international standards are acceptable to the United States Environmental Protection Agency and Food and Drug Administration, and fulfil the requirements of 40 CFR Part 160, 40 CFR Part 792 and 21 CFR Part 58 (as amended).

..... DATE: 1-8-94

D.J. Allen B.Sc. (Hons)
Study Director
for Safepharm Laboratories

CONTENTS

C O N T E N T S (continued)

SUMMARY

STUDY SPONSOR : MITSUBISHI-KASEI INSTITUTE OF TOXICOLOGICAL & ENVIRONMENTAL SCIENCES

PROJECT NUMBER : 388/114

TEST MATERIAL : [NW4RO]

1. A study was performed to assess the skin contact sensitisation potential of the test material in the albino guinea pig. The method used followed that described in the OECD Guidelines for Testing of Chemicals No. 406 "Skin Sensitisation" (adopted 17 July 1992) and Method B6 of Commission Directive 92/69/EEC (which constitutes Annex V of Council Directive 67/548/EEC).

   The results may be used as a basis for classification and labelling under Annex VI of Council Directive 67/548/EEC (as adapted to technical progress by Commission Directive 91/325/EEC).

2. Ten test and ten control animals were used for the main study.

   Based on the results of sighting tests, the concentrations of test material for the induction and challenge phases were selected as follows:

Intradermal Induction	:	1% w/v in distilled water
Topical Induction	:	50% w/w in distilled water
Topical Challenge	:	25% and 10% w/w in distilled water

3. The test material produced a 100% (10/10) sensitisation rate and was classified as an extreme sensitiser to guinea pig skin. The test material was also classified as a sensitiser according to EC labelling regulations. The risk phrase R 43 "MAY CAUSE SENSITISATION BY SKIN CONTACT" is required.

PROJECT NUMBER: 388/114

[NW4RO:]

MAGNUSSON & KLIGMAN MAXIMISATION

STUDY IN THE GUINEA PIG

1. INTRODUCTION

This study was performed to assess the skin contact sensitisation potential of the test material (Safepharm Standard Method Number OECD 75). The method used followed the recommendations of the OECD Guidelines for the Testing of Chemicals No. 406 "Skin Sensitisation" (adopted 17 July 1992) and Method B6 of Commission Directive 92/69/EEC (which constitutes Annex V of Council Directive 67/548/EEC).

The results may be used as a basis for classification and labelling under Annex VI of Council Directive 67/548/EEC (as adapted to technical progress by Commission Directive 91/325/EEC).

The test system was chosen because the guinea pig has been shown to be a suitable species for this type of study and is recommended in the test method. The strain used in these laboratories has been shown to produce satisfactory sensitisation responses using known positive sensitisers (see Appendix XI). The results of the study are believed to be of value in predicting the likely contact sensitisation potential of the test material to man.

The study was conducted in accordance with the internationally accepted general principles of Good Laboratory Practice and Safepharm Standard Operating Procedures.

The study was performed between 26 April 1994 and 5 June 1994.

2. TEST MATERIAL

2.1 Description, Identification and Storage Conditions

The test material was supplied by the study sponsor as follows:

Sponsor's identification	:	[NW4RO]
Batch number	:	002
Date received	:	7 April 1994
Description	:	dark maroon powder
Container	:	opaque plastic jar
Storage conditions	:	room temperature

Data relating to the identity, purity and stability of the test material are the responsibility of the sponsor.

2.2 Method of Preparation

For the purpose of this study the test material was freshly prepared as follows:

Intradermal Induction	:	1% w/v in distilled water 1% w/v in a mixture of Freund's Complete Adjuvant plus distilled water (1:1)
Topical Induction	:	50% w/w in distilled water
Topical Challenge	:	25% and 10% w/w in distilled water

Determination by analysis of the concentration, homogeneity and stability of the test material preparations was not appropriate because it was not specified in the Study Plan and is not a requirement of the Test Guideline.

3. TEST SYSTEM

3.1 Specification

Twenty-six female, albino Dunkin-Hartley guinea pigs were supplied by David Hall Limited, Burton-on-Trent, Staffordshire, U.K. At the start of the main study the animals weighed 358 - 418g, and were approximately eight to twelve weeks old. After a minimum acclimatisation period of five days, each animal was selected at

3. TEST SYSTEM (contd)

3.1 Specification (contd)

random and given a number unique within the study which was written on a small area of clipped rump using a black indelible marker-pen.

3.2 Husbandry

The animals were housed singly or in pairs in solid-floor polypropylene cages furnished with woodflakes. Free access to mains tap water and food (Guinea Pig FD1 Diet, Special Diets Services Limited, Witham, Essex, U.K.) was allowed throughout the study.

The animal room was maintained at a temperature of 20 - 23°C and relative humidity of 52 - 61%. The rate of air exchange was approximately 15 changes per hour and the lighting was controlled by a time switch to give 12 hours light and 12 hours darkness.

4. PROCEDURE

The method used for assessing the sensitising properties of the test material was based on the Guinea Pig Maximisation test of Magnusson B. & Kligman A.M., J. Invest. Dermatol. (1969) 52: 268 - 276.

4.1 Selection of Concentrations for Main Study (Sighting Tests)

The concentrations of test material to be used at each stage of the main study were determined by 'sighting tests' in which groups of guinea pigs were treated with various concentrations of test material. The procedures were as follows:

a) Selection of Concentration for Intradermal Induction

Two animals were intradermally injected with preparations of test material (1% or 5% w/v in distilled water). The degree of erythema at the injection sites was assessed approximately 24, 48 and 72 hours and 7 days after injection according to the Draize scale shown in Appendix X. The degree of oedema was not evaluated. Any evidence of systemic toxicity was also recorded. The highest concentration that caused only mild to moderate skin irritation and was well tolerated systemically, was selected for the intradermal induction stage of the main study.

4. PROCEDURE (contd)

4.1 Selection of Concentrations for Main Study (Sighting Tests) (contd)

b) Selection of Concentration for Topical Induction

Two guinea pigs (intradermally injected with Freund's Complete Adjuvant nine days earlier) were treated with four preparations of the test material (50%, 25%, 10% and 5% w/w in distilled water).

The highest concentration producing only mild to moderate dermal irritation after a 48-hour occlusive exposure, was selected for the topical induction stage of the main study.

c) Selection of Concentration for Topical Challenge

Four preparations of the test material (50%, 25%, 10% and 5% w/w in distilled water) were applied occlusively to the flanks of two guinea pigs for a period of 24 hours. These guinea pigs did not form part of the main study but had been treated identically to the control animals of the main study, up to Day 14. The highest non-irritant concentration of the test material and one lower concentration were selected for the topical challenge stage of the main study.

4.2 Main Study

A group of twenty guinea pigs was used for the main study, ten test and ten control. The bodyweight of each animal was recorded at the start and end of the study.

Two main procedures were involved in the maximisation test; (a) an induction of a response and (b) a challenge of that response.

a) Induction

Induction of the Test Animals: Shortly before treatment on Day 0 the hair was removed from an area approximately 40 mm x 60 mm on the shoulder region of each animal with veterinary clippers. A row of three injections (0.1 ml each) was made on each side of the mid-line. The injections were:

4. PROCEDURE (contd)

4.2 Main Study (contd)

a) Induction (contd)

Induction of the Test Animals (contd)

i) Freund's Complete Adjuvant plus distilled water in the ratio 1:1.
ii) a 1% w/v dilution of test material in distilled water.
iii) a 1% w/v dilution of test material in a 1:1 preparation of Freund's Complete Adjuvant plus distilled water.

Approximately 24 and 48 hours after intradermal injection the degree of erythema at the test material injection sites (i.e. injection site ii) was evaluated according to the scale shown in Appendix X.

One week later (Day 7), the same area on the shoulder region used previously for intradermal injections was clipped again and treated with a topical application of the test material formulation (50% w/w in distilled water). The test material formulation was applied as a thick, even layer on filter paper (WHATMAN No.4: approximate size 40 mm x 20 mm) which was held in place by a strip of surgical adhesive tape (BLENDERM: approximate size 50 mm x 30 mm) and covered with an overlapping length of aluminium foil. The patch and foil were further secured by a strip of elastic adhesive bandage (ELASTOPLAST: approximate size 250 mm x 35 mm) wound in a double layer around the torso of each animal. This occlusive dressing was kept in place for 48 hours.

The degree of erythema and oedema was quantified one and twenty-four hours following removal of the patches using the scale shown in Appendix X.

Any other reactions were also recorded.

4. PROCEDURE (contd)

4.2 Main Study (contd)

Induction of the Control Animals: Intradermal injections were administered using an identical procedure to that used for the test animals, except that the injections were:

i) Freund's Complete Adjuvant plus distilled water in the ratio 1:1.
ii) distilled water.
iii) 50% w/v formulation of distilled water in a 1:1 mixture of Freund's Complete Adjuvant/distilled water.

The topical applications followed the same procedure as for the test animals except that the vehicle alone was applied to the filter paper. Skin reactions were quantified as for the test animals.

b) Challenge

Shortly before treatment on Day 21, an area, approximately 50 mm x 70 mm on both flanks of each animal, was clipped free of hair with veterinary clippers.

A square of the filter paper (WHATMAN No. 4: approximate size 20 mm x 20 mm) was saturated with the test material formulation (25% w/w in distilled water) and applied to the shorn right flank of each animal. The filter paper patch was held in place by a strip of surgical adhesive tape (BLENDERM: approximate size 40 mm x 50 mm). To ensure that the maximum non-irritant concentration was used at challenge, the test material at a concentration of 10% w/w in distilled water was also similarly applied to a separate skin site on the left shorn flank. The patches were occluded with an overlapping length of aluminium foil and secured by a strip of elastic adhesive bandage (ELASTOPLAST: approximate size 250 mm x 75 mm) wound in a double layer around the torso of each animal.

4. PROCEDURE (contd)

4.2 Main Study (contd)

b) Challenge (contd)

After 24 hours, the dressing was carefully cut using blunt-tipped scissors, removed and discarded. The challenge sites were swabbed with cotton wool soaked in distilled water to remove residual material. The position of the treatment sites was identified by using a black indelible marker-pen.

Prior to the 24-hour observation the flanks were clipped using veterinary clippers to remove regrown hair.

c) Evaluation of Skin Reactions

Approximately 24 and 48 hours after challenge dressing removal, the degree of erythema and oedema was quantified using the scale shown in Appendix X.

Any other reactions were also recorded.

5. EVALUATION OF DATA

The percentage of test animals that showed a more severe reaction at the test material challenge site than the most severe reaction seen in the control animals, was compared with the following scale:

% of animals sensitised	Classification of sensitisation potential
0	non-sensitiser
> 0 - 8	weak sensitiser
> 8 - 28	mild sensitiser
> 28 - 64	moderate sensitiser
> 64 - 80	strong sensitiser
> 80 - 100	extreme sensitiser

The data obtained may be used to classify the test material under the Council Directive 67/548/EEC, as amended by Commission according to Directive 91/325/EEC, on the classification, packaging and labelling of dangerous substances. These classification criteria are also in the UK Approved Code of Practice "Classification and Labelling of Substances Dangerous for Supply".

7. RESULTS

7.1 Intradermal and Topical Sighting Tests

A summary of the results of the intradermal sighting test and the individual skin reactions observed in the topical sighting tests are given in Appendices I, II and III.

Based on these results, the following concentrations were selected for the main study:

Intradermal Induction	:	1% w/v in distilled water
Topical Induction	:	50% w/w in distilled water
Topical Challenge	:	25% and 10% w/w in distilled water

7.2 Main Study

a) Skin Reactions Observed After Intradermal Induction

Individual reactions observed at the intradermal induction sites of test and control group animals are given in Appendices IV and V.

Slight purple-coloured staining was commonly noted at the intradermal induction sites of test group animals at the 24 and 48-hour observations. The staining did not affect evaluation of erythema.

Very slight to well-defined erythema was noted at the intradermal induction sites of all test group animals at the 24-hour observation and in seven test group animals at the 48-hour observation. Very slight erythema was noted at the intradermal induction sites of nine control group animals at the 24-hour observation and in three control group animals at the 48-hour observation.

b) Skin Reactions Observed After Topical Induction

Individual reactions observed at the topical induction sites of test and control group animals are given in Appendices VI and VII.

Brown-coloured staining was noted at the induction sites of all test group animals at the 1 and 24-hour observations. The staining prevented accurate evaluation of erythema at the induction sites of all test group animals at the 1-hour observation and in five test group animals at the 24-hour observation.

7. RESULTS (contd)

7.2 Main Study (contd)

b) Skin Reactions Observed After Topical Induction (contd)

Very slight oedema was noted at the induction sites of nine test group animals at the 1-hour observation. Very slight erythema was noted at the induction sites of four test group animals at the 24-hour observation. Red/brown-coloured residual test material was commonly noted.

No skin reactions were noted at the treatment sites of control group animals at the 1 and 24-hour observations.

c) Skin Reactions Observed After Topical Challenge

Individual reactions at the challenge sites of test and control group animals are given in Tables 1 and 2.

Staining was noted at the challenge sites of all test and control group animals at the 24 and 48-hour observations. The staining did not affect evaluation of skin responses.

25% w/w in Distilled Water

Positive skin responses, very slight to well-defined erythema (grades 1 or 2) were noted at the challenge sites of all test group animals at the 24-hour observation. Very slight erythema was noted at the challenge sites of four test group animals at the 48-hour observation.

No skin reactions were noted at the challenge sites of control group animals at the 24 and 48-hour observations.

10% w/w in Distilled Water

Positive skin responses, very slight to well-defined erythema (grades 1 or 2) were noted at the challenge sites of six test group animals at the 24-hour observation.

No skin reactions were noted at the challenge sites of control group animals at the 24 and 48-hour observations.

7. RESULTS (contd)

7.3 Bodyweight

Individual bodyweights and bodyweight gains of test and control group animals are given in Appendices VIII and IX.

Bodyweight gains of guinea pigs in the test group, between Day 0 and Day 24, were comparable to those observed in the control group animals over the same period.

8. CONCLUSION

The test material, [NW4RO], produced a 100% (10/10) sensitisation rate and was classified as an EXTREME SENSITISER to guinea pig skin. The test material was also classified as a sensitiser according to EC labelling regulations. The risk phrase R 43 "MAY CAUSE SENSITISATION BY SKIN CONTACT" is required.

NW4RO: MAGNUSSON & KLIGMAN MAXIMISATION STUDY IN THE GUINEA PIG

TABLE 1 INDIVIDUAL SKIN REACTIONS IN TEST ANIMALS AT CHALLENGE

CHALLENGE CONCENTRATIONS: 25% AND 10% w/w VEHICLE: DISTILLED WATER

Animal Number	Skin Reactions (Hours After Removal of Dressing) 24 hours						48 hours					
	25%			10%			25%			10%		
	Er	Oe	Other	Er	Oe	Other	Er	Oe	Other	Er	Oe	Other
1	2	0	STA	0	0	STA	1	0	STA	0	0	STA
2	2	0	STA	1	0	STA	0	0	STA	0	0	STA
3	2	0	STA	1	0	STA	1	0	STA	0	0	STA
4	2	0	STA	0	0	STA	0	0	STA	0	0	STA
5	2	0	STA	1	0	STA	0	0	STA	0	0	STA
6	2	0	STA	1	0	STA	1	0	STA	0	0	STA
7	1	0	STA	0	0	STA	0	0	STA	0	0	STA
8	1	0	STA	1	0	STA	0	0	STA	0	0	STA
9	2	0	STA	2	0	STA	1	0	STA	0	0	STA
10	1	0	STA	0	0	STA	0	0	STA	0	0	STA

Er = erythema Oe = oedema STA = staining

NW4RO: MAGNUSSON & KLIGMAN MAXIMISATION STUDY IN THE GUINEA PIG

TABLE 2 INDIVIDUAL SKIN REACTIONS IN CONTROL ANIMALS AT CHALLENGE

CHALLENGE CONCENTRATIONS: 25% AND 10% w/w VEHICLE: DISTILLED WATER

Animal Number	Skin Reactions (Hours After Removal of Dressing) 24 hours						48 hours					
	25%			10%			25%			10%		
	Er	Oe	Other	Er	Oe	Other	Er	Oe	Other	Er	Oe	Other
11	0	0	STA	0	0	STA	0	0	STA	0	0	STA
12	0	0	STA	0	0	STA	0	0	STA	0	0	STA
13	0	0	STA	0	0	STA	0	0	STA	0	0	STA
14	0	0	STA	0	0	STA	0	0	STA	0	0	STA
15	0	0	STA	0	0	STA	0	0	STA	0	0	STA
16	0	0	STA	0	0	STA	0	0	STA	0	0	STA
17	0	0	STA	0	0	STA	0	0	STA	0	0	STA
18	0	0	STA	0	0	STA	0	0	STA	0	0	STA
19	0	0	STA	0	0	STA	0	0	STA	0	0	STA
20	0	0	STA	0	0	STA	0	0	STA	0	0	STA

Er = erythema Oe = oedema STA = staining

A P P E N D I C E S

NW4RO: MAGNUSSON & KLIGMAN MAXIMISATION STUDY IN THE GUINEA PIG

APPENDIX I INTRADERMAL SIGHTING TEST - SUMMARY OF RESULTS

VEHICLE: DISTILLED WATER

Animal Identification	Time of Observation	Concentration of Test Material (% w/v)	Grade of Erythema at Injection Sites	Evidence of Systemic Toxicity
A	24 hours	1	1-2	None
	48 hours		2	None
	72 hours		2	None
	7 days		1-2	None
B	24 hours	5	2-4 Focal Eschar	None
	48 hours		2-4 Focal Eschar	None
	72 hours		2-4 Focal Eschar	None
	7 days		2-4 Focal Eschar	None

The concentration of the test material selected for the intradermal induction stage of the main study was 1% w/v in distilled water

NW4RO: MAGNUSSON & KLIGMAN MAXIMISATION STUDY IN THE GUINEA PIG

APPENDIX II

TOPICAL SIGHTING TEST FOR INDUCTION APPLICATION

(48-HOUR EXPOSURE) - INDIVIDUAL SKIN REACTIONS

VEHICLE: DISTILLED WATER

Animal Identification	Concentration of Test Material (% w/w)	Skin Reactions (Hours After Removal of Patches)								
		1			24			48		
		Er	Oe	Other	Er	Oe	Other	Er	Oe	Other
C	50<	?s	2	-	?s	1	-	?s	0	-
	25	?s	0	-	1	0	-	1	0	-
	10	?s	1	-	0	0	-	0	0	-
	5	?s	0	-	0	0	-	0	0	-
D	50<	?s	1	-	1	0	-	0	0	-
	25	?s	0	-	1	0	-	0	0	-
	10	?s	0	-	0	0	-	0	0	-
	5	?s	0	-	0	0	-	0	0	-

Er = erythema Oe = oedema - = no other reactions noted
?s = yellow/orange-coloured staining prevents accurate evaluation of erythema
< Maximum attainable concentration suitable for topical application

The concentration of the test material selected for the main study topical induction was 50% w/w in distilled water

NW4RO: MAGNUSSON & KLIGMAN MAXIMISATION STUDY IN THE GUINEA PIG

APPENDIX III TOPICAL SIGHTING TEST FOR CHALLENGE APPLICATION

(24-HOUR EXPOSURE) - INDIVIDUAL SKIN REACTIONS

VEHICLE: DISTILLED WATER

Animal Identification	Concentration of Test Material (% w/w)	Skin Reactions (Hours After Removal of Patches)								
		1			24			48		
		Er	Oe	Other	Er	Oe	Other	Er	Oe	Other
E	50<	?s	1	-	1	0	STA	1	0	STA
	25	?s	1	-	0	0	STA	0	0	STA
	10	1	0	STA	0	0	STA	0	0	STA
	5	1	0	STA	0	0	STA	0	0	STA
F	50<	?s	1	-	0	0	STA	0	0	STA
	25	?s	0	-	0	0	STA	0	0	STA
	10	1	0	STA	0	0	STA	0	0	STA
	5	?s	0	-	0	0	STA	0	0	STA

Er = erythema Oe = oedema - = no other reactions noted STA = slight pale brown-coloured staining
?s = brown-coloured staining prevents accurate evaluation of erythema
< Maximum attainable concentration suitable for topical application

The concentrations of the test material selected for the main study topical challenge were 25% and 10% w/w in distilled water

NW4RO: MAGNUSSON & KLIGMAN MAXIMISATION STUDY IN THE GUINEA PIG

APPENDIX IV INTRADERMAL INDUCTION - INDIVIDUAL SKIN REACTIONS IN TEST ANIMALS

INTRADERMAL INDUCTION CONCENTRATION: 1% w/v

VEHICLE: DISTILLED WATER

Animal Number	Skin Reactions at Observation Time: 24 hours		48 hours	
	Left Side	Right Side	Left Side	Right Side
1	2 STA	1	2 STA	1
2	2 STA	1	1 STA	1
3	1 STA	1 STA	1 STA	1 STA
4	1 STA	1 STA	1 STA	1 STA
5	1 STA	1	0 STA	0
6	1 STA	1 STA	0 STA	0 STA
7	1 STA	1 STA	0 STA	0 STA
8	1 STA	1 STA	1 STA	1 STA
9	1	1	1	0
10	1 STA	1 STA	1 STA	1 STA

STA = slight purple-coloured staining

NW4RO: MAGNUSSON & KLIGMAN MAXIMISATION STUDY IN THE GUINEA PIG

APPENDIX V INTRADERMAL INDUCTION - INDIVIDUAL SKIN REACTIONS IN CONTROL ANIMALS

VEHICLE: DISTILLED WATER

Animal Number	Skin Reactions at Observation Time: 24 hours		48 hours	
	Left Side	Right Side	Left Side	Right Side
11	1	0	0	0
12	0	0	0	0
13	1	1	0	0
14	1	1	0	0
15	1	1	1	0
16	1	1	0	0
17	1	1	0	0
18	1	1	1	1
19	1	1	0	0
20	1	1	1	1

NW4RO: MAGNUSSON & KLIGMAN MAXIMISATION STUDY IN THE GUINEA PIG

APPENDIX VI TOPICAL INDUCTION - INDIVIDUAL SKIN REACTIONS IN TEST ANIMALS

INDUCTION CONCENTRATION: 50% w/w

VEHICLE: DISTILLED WATER

Animal Number	Skin Reactions (Hours After Removal of Dressing)					
	1 hour			24 hours		
	Er	Oe	Other	Er	Oe	Other
1	?s	1	Rt	?s	0	-
2	?s	1	Rt	1	0	STA
3	?s	1	Rt	?s	0	-
4	?s	0	Rt	1	0	STA
5	?s	1	Rt	?s	0	Rt
6	?s	1	Rt	1	0	STA
7	?s	1	Rt	?s	0	Rt
8	?s	1	Rt	?s	0	-
9	?s	1	Rt	1	0	STA
10	?s	1	Rt	0	0	STA

Er = erythema Oe = oedema - = no other reactions noted STA = brown-coloured staining

?s = brown-coloured staining prevents accurate evaluation of erythema

Rt = red/brown-coloured residual test material

NW4RO: MAGNUSSON & KLIGMAN MAXIMISATION STUDY IN THE GUINEA PIG

APPENDIX VII TOPICAL INDUCTION - INDIVIDUAL SKIN REACTIONS IN CONTROL ANIMALS

VEHICLE: DISTILLED WATER

Animal Number	Skin Reactions (Hours After Removal of Dressing)					
	1 hour			24 hours		
	Er	Oe	Other	Er	Oe	Other
11	0	0	-	0	0	-
12	0	0	-	0	0	-
13	0	0	-	0	0	-
14	0	0	-	0	0	-
15	0	0	-	0	0	-
16	0	0	-	0	0	-
17	0	0	-	0	0	-
18	0	0	-	0	0	-
19	0	0	-	0	0	-
20	0	0	-	0	0	-

Er = erythema Oe = oedema - = no dermal reactions noted

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Susan P. Engelman
Vice President
Environmental Health & Safety Affairs
Hoechst Celanese Corporation
Route 202-206
P.O. Box 2500
Somerville, New Jersey 08876-1258

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAR 30 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). **Please cite the assigned 8(e) number when submitting follow-up or supplemental information** and refer to the reverse side of this page for "EPA Information Requests".

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

13242A

EPA INFORMATION REQUESTS

Document ID: 8EHQ-1094-13239
8EHQ-1094-13242

EPA requests:

1. [ ] No additional information at this time.

2. [ ] Additional information or clarification on

3. [ ] A full copy of the final report (including the actual experimental protocol, applicable results of gross or histopathologic examinations, data, results of any statistical analyses, etc.) from each study mentioned in your submission.

4. [✓] A description of all voluntary actions taken by your company in response to the findings indicated in your submission.

5. [ ] A complete copy of the current and/or revised Material Safety Data Sheets and labels for the following chemical(s) listed in your submission:

_____ _____

_____ _____

_____ _____

6. [ ]

Please direct questions regarding these requests to Mr. Terry O'Bryan (202-260-3483) or Mr. John Myers (202-260-3543) of the OPPT Risk Analysis Branch.

Triage of 8(e) Submissions

Date sent to triage: _____ NON-CAP CAP

Submission number: 13242A TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX	CTOX	EPI	RTOX	GTOX
STOX/ONCO	CTOX/ONCO	IMMUNO	CYTO	NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: (0) 1 2 **pages** 1 **pages** 1, tabs

Notes:

Contractor reviewer : LPS **Date:** 12/13/94.

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ-1094-13242 SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: Hoechst Celanese Corporation

SUB. DATE: 10/21/94 10/28/94 CSRAD DATE: 11/18/94

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER/CUSTOMERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

CHEMICAL NAME:

CAS#
13301-61-6

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
(0228)	ALLERG (ANIMAL)	01 (02) 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
(0243)	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA:

NON-CBI INVENTORY: (YES) NO IN TSCA INV

ONGOING REVIEW: YES (DROP/REFER) NO (CONTINUE) REFER

SPECIES: GP

TOXICOLOGICAL CONCERN: LOW MED (HIGH) Dermal Sensitization

USE:

PRODUCTION:

CAS SR

COMMENTS: Non-CAP

13242A

H

Dermal sensitization in guinea pigs is of high concern based on a 100% (10/10) positive response following a challenge concentration of 25% using the Magnusson and Kligman maximization test.